

REMARKS/ARGUMENTS

Upon entry of the present amendment, claims 1, 7-19, 30 and 31 will be pending in the application and presented for examination. Claims 2-6 and 20-29 have been canceled without prejudice or disclaimer. Claims 8, 9 and 13 have been amended. No new matter has been introduced with the foregoing amendments.

Reconsideration is respectfully requested in view of the amendment to the claims and the following remarks. For the Examiner's convenience, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

I. FORMALITIES

Support for the amendments to claims 8, 9 and 13 is found throughout the specification as filed. More particularly, claim 8 has been amended to more particularly claim the subject matter Applicants regard as their invention. Support for the amendment to claim 9 is found, *inter alia*, in claim 8 as filed. Support for the amendment to claim 13 is found, *inter alia*, on page 21, line 21. Applicants submit that no new matter has been introduced in the amendments to the claims. Entry is respectfully requested.

II. REJECTION UNDER 35 U.S.C § 112, SECOND PARAGRAPH

The Examiner has rejected claims 8, 9, and 13-19 under 35 U.S.C § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner alleges that claim 8 is indefinite for reciting the phrase "wherein Y of reactant (B) in step (iv) is absent or is" when the reactant (B) in step (iv) has no "Y" group. The Examiner alleges that the recitation of "derivative resin (TB)" in claim 9 lacks antecedent basis. The Examiner further alleges that the recitation of the phrase "represented by the formula (ID)" in claim 13 is vague as no structural formula is present in the claim or in the claim the claim 13 dependent from. Applicants have amended claims 8, 9 and 13, and to the extent that the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

Applicants have amended claim 8 to delete the phrases "of reactant (B) in step (iv)" as well as "and R1 is hydroxyl." Claim 8 now clearly sets forth that the Y group is -CH₂- or is absent and X is oxygen. In addition, Applicants have amended claim 9, which is dependent on claim 8, to correct a typographical error. Specifically, the reference in claim 9 to the phrase "derivatized resin (TB)" has been amended to now recite "derivatized resin (IB)". Finally, Applicants have amended claim 13 to set forth the structural formula of a compound having formula (ID). In view of the amendments to the claims, Applicants submit that claims 8, 9 and 13 are fully compliant with 35 U.S.C. § 112, second paragraph. As such, Applicants respectfully request the rejection of claims 8, 9 and 13 and the claims dependent thereon, be withdrawn.

III. REJECTION UNDER 35 U.S.C. § 103(a)

The Examiner has rejected method claims 1 and 30 as allegedly being obvious over the combined teachings of O'Shannessy *et al.* (U.S. Patent No. 4,874,813, "O'Shannessy"), Carey *et al.* (Carey, F. A.; Sundberg, R.J., *Advanced Organic Chemistry* 3rd Ed., New York, Plenum Press, 1990, p.146-7, "Carey"), and Chu *et al.* (U.S. Patent No. 3,873,514, "Chu"). The Examiner alleges that the combination of O'Shannessy, Carey and Chu teach Applicants' method for making the claimed resin of Formula I wherein R₄ is NH₂, X is oxygen, Y is absent and Z is oxygen. The Examiner alleges that although O'Shannessy's method does not disclose the use of a compound of formula R₁-(C=X)-R₂, in which X is oxygen, Chu and Carey combined teach the equivalence of a carbodiimide and a R₁-(C=X)-R₂, wherein X is oxygen. The Examiner further alleges that the fact that Shannessy's method contains an additional step to form a succinimide ester intermediate is irrelevant as Applicants use the "comprising" terminology in their claim language and thus more method steps may be added. In response, Applicants respectfully traverse the rejection.

1. No *Prima Facie* Case of Obviousness Exists

As set forth in M.P.E.P. § 2143:

[t]o establish a *prima facie* case of obviousness, *three* basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the

art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

All three elements set forth above must be present in order to establish a *prima facie* case of obviousness. Applicants assert that a *prima facie* case of obviousness has not been established as there is no suggestion or motivation to modify the references.

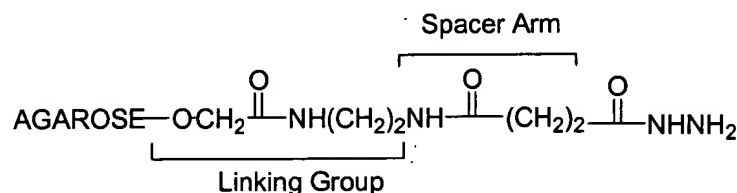
2. There is No Suggestion or Motivation to Modify the References

Applicants state that there is simply no motivation or suggestion provided in the cited references to modify their teaching in the way the Examiner has contemplated.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

O'Shannessy discloses a method for making an intermediate having: 1) an agarose solid support, 2) a linking molecule, 3) a spacer molecule and 4) a hydrazide group, and has for example, the formula shown in Figure 1 (reproduced below for the Examiner's convenience).

Figure 1: O'Shannessy's Acyl Hydrazine 1 (see, column 6, lines 50-55, O'Shannessy)

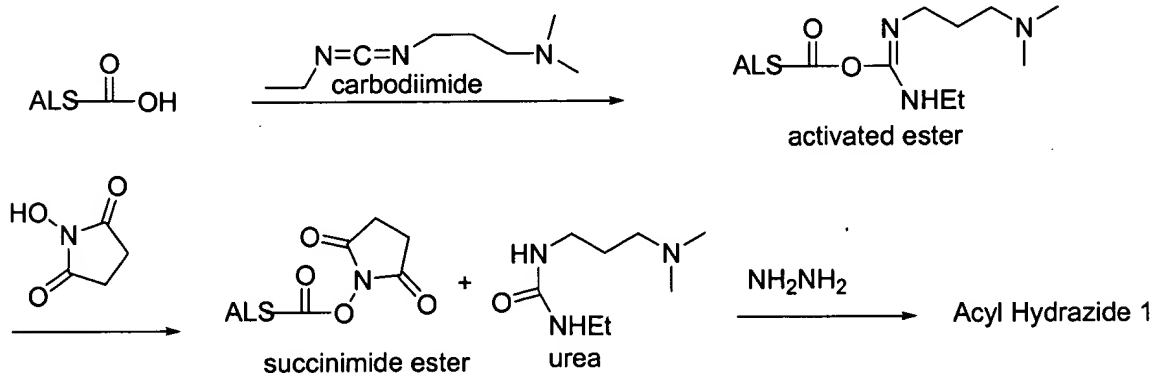


O'Shannessy and Chu combined disclose a method for preparing acyl hydrazine 1 in which a carboxylic acid is activated with a carbodiimide and the resultant activated ester is

displaced by N-hydroxysuccinimide to form the succinimide ester. The succinimide ester is then displaced by hydrazine to form acyl hydrazine 1 (*see*, Figure 2).

Figure 2: O'Shannessy's Method for Making Acyl Hydrazine 1

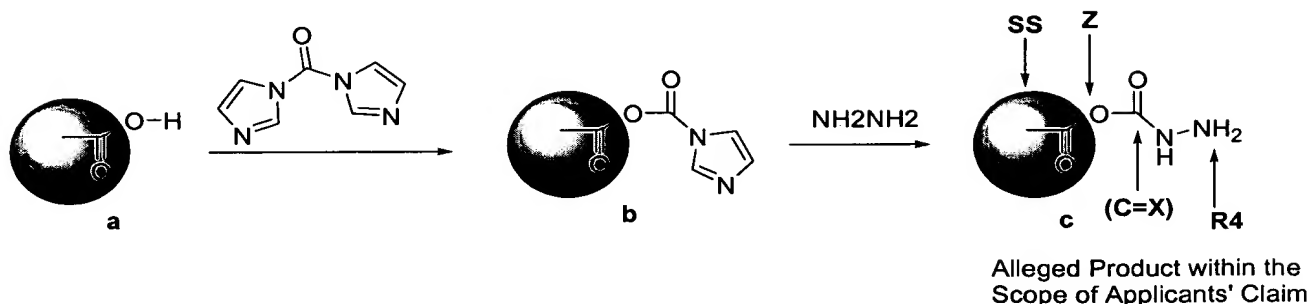
Agarose and Linking group and Spacer arm = ALS



The Examiner alleges that Carey teaches the equivalence of a carbodiimide and a R1-(C=X)-R2 group, wherein X is oxygen. Based on the combined teachings of O'Shannessy, Chu and Carey, the Examiner alleges that Applicants' method is obvious and sets forth the following scenario to illustrate how the cited references, when combined, give rise to the instantly claimed method (*see*, page 6, lines 7-21, Paper No. 28).

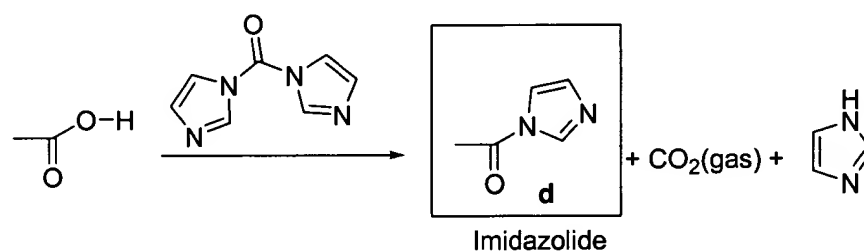
In the Examiner's scenario, briefly described here and depicted below in Figure 3, R-Y-Z-SS (a) contains an agarose/linker solid support, terminal oxygen for Z, no Y, and hydrogen for R (*i.e.*, R-Y represents the terminal hydroxyl group of the carboxylic acid). The R group is deprotonated to allow the oxygen atom to react with R1-(C=X)-R2 wherein, R1 and R2 are imidazolyl and X is oxygen to form an imidazolide intermediate, R1-(C=X)-Y-Z-SS (b), wherein R1 is imidazolyl, X is oxygen, Y is absent and Z is oxygen. This intermediate is then reacted with hydrazine to yield a compound c, allegedly having Applicants' formula I (R4-NH-(C=X)-Y-Z-SS) c, in which R4 is NH₂, X is oxygen, Y is absent and Z is oxygen. Applicants respectfully disagree with this proposed analysis.

Figure 3: Examiner's Scenario



Applicants assert that the scenario proposed by the Examiner does not produce product c, a product that allegedly falls within the scope of Applicants' claim. As clearly shown on page 147 of Carey, and reproduced in Figure 4 below, the reaction between a carboxylic acid (RCOOH) and carbonyldiimidazole (R₁-(C=O)-R₂), will produce an imidazolide d (see, highlighted box in Figure 4), not compound b, as proposed by the Examiner. Applicants respectfully point out the Examiner may have mistakenly referred to b (in Figure 3) as an imidazolide. Entropy is the driving force for this reaction as the formation of the imidazolide d (in Figure 4) also results in the release of carbon dioxide gas and imidazole.

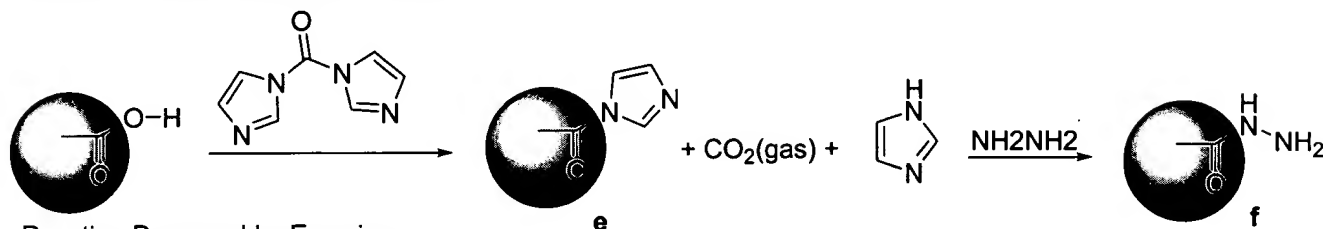
Figure 4: Teaching of Cary



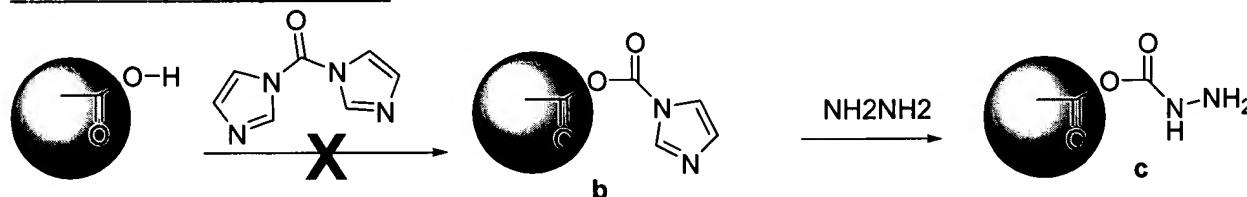
Therefore, the teaching of O'Shannessy, Chu and Carey, as applied to the scenario suggested by the Examiner, would actually produce imidazolide e which would further react with the hydrazine to provide acyl hydrazine f (see, Figure 5) which is NOT a product within the scope of Applicants' formula I.

Figure 5: Reaction with Carboxylic Acid and Carbonyldiimidazole

Reaction Supported by Carey Reference



Reaction Proposed by Examiner



Applicants submit that the product resulting from the scenario proposed by the Examiner would be an acyl hydrazine **f**, which simply does not fall within the scope of Applicants' formula I. Therefore, the proposed combination of the teachings of O'Shannessy, Chu and Carey, *does not teach or suggest Applicants' compounds*. As such, Applicants submit that it is implausible to consider that one skilled in the art would be motivated to modify the reference of O'Shannessy in combination with Chu and/or Carey to arrive at the presently claimed method. Applicants submit that no *prima facie* case of obviousness has been established. Accordingly, Applicants respectfully request that the rejection of the claims be withdrawn.

IV. CONCLUSION

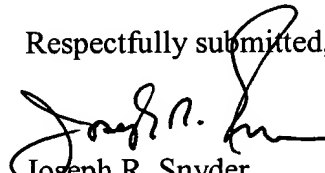
In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Appl. No. 09/122,576
Amdt. dated November 21, 2003
Reply to Office Action of August 21, 2003

PATENT

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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